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| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/373,938 | Hallenbeck et al. |
| **Examiner** | **Group Art Unit** |
| Gai (Jennifer) Mi Lee | 1632 |

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claim**

☒ Claim(s) 1-31 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-31 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

**This application contains sequence disclosures that are encompassed by the definition s for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Application. Until these requirements are satisfied, the applicant remains in non-compliance with the sequence rules. Please refer to the attached notice to comply.**

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention

Claims 4-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a tumor or metastases by a direct intratumor administration of an adenoviral vector comprising a full length cDNA sequence encoding murine endostatin for expression of said endostatin, does not reasonably provide enablement for any and all methods of delivery in any and all host with an adenoviral vector comprising any and all DNA sequences encoding endostatin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method of providing expression of endostatin in any and all host comprising an adenoviral vector including any and all DNA sequence encoding endostatin; a

method of treating tumor in any and all host comprising an adenoviral vector including any and all DNA sequence encoding endostatin; a method of treating tumor metastases comprising an adenoviral vector including any and all DNA sequence encoding endostatin; and a method of treating colon cancer metastases in any and all host comprising an adenoviral vector including any and all DNA sequence encoding endostatin by any and all methods of delivery.

The claimed invention is directed to effecting gene therapy by way of delivering an adenoviral vector comprising secretion signal peptide, Ig-Kappa, immediately 5' of the DNA sequence encoding endostatin in any and all hosts by any and all routes of administration of an adenoviral vector comprising any and all DNA encoding endostatin, and achieving "treatment" via gene therapy of any and all tumor or tumor metastases. While, in the Examples, the specification teaches that *in vitro* cellular assays to exhibit a level of expression and delivery of adenoviral vector is detected by the circulating presence of secreting endostatin; the specification fails to provide a correlation to treating any and all tumor and tumor metastases in any and all hosts by any and all routes of administration of an adenoviral vector comprising any and all DNA encoding endostatin to exhibit expression as therapy. The specification discloses that no drug resistance or side effects were reported but like most angiogenic inhibitors, it functions through cytostatic rather cytotoxic effect, relying on a prolonged maintenance of an anti-angiogenesis state (p. 2, paragraph 2). The specification further disclose that the molecular mechanism of endostatin induced anti-angiogenesis is not clear (page 2, paragraph 3). The specification states that by inhibiting, preventing, or destroying the growth of endothelial cells of the tumor, the

endostatin stops the blood supply to tumor cells, thereby inhibiting, preventing, or destroying the growth of the metastasized tumor (p. 14, paragraph 2).

With regards to the state of the art in endostatin anti-angiogenesis, Cirri et al ((Oct.-Dec. 1999) International J. Of Biological Markers, Vol. 14 (4): 263-7)) state that endostatin seems to have endothelial cell-specific activity, since it inhibits the proliferation of endothelial cells in vitro while it has no direct effect on tumor cells or non-endothelial cell types such as fibroblasts and smooth muscle cells (p. 264, column 2). Cirri et al further state that the mechanism by which endostatin inhibits endothelial cell proliferation, migration and angiogenesis is still to be determined (p. 264, column 2). Harris et al ((May 30, 1998) Lancet, Vol. 351 (9116): 1598-9) state that the receptors or targets are unknown and may not be expressed on human tumour vessels or to the same extent as in murine vessels. The animal tumours were very small compared with the tumours in patients eligible for phase I trials. The human pharmacokinetics may make the proteins difficult to deliver, and if receptors or mechanisms were known, more appropriate drugs may be developed. Harris et al thus state that these proteins are far from being ready for clinical use (p. 1599, column 1). Kerbel R S ((Nov. 27, 1997) Nature, Vol. 390 (6658): 335-6) further state that long experience tells us to be cautious in equating the results of experiments using tumours in mice to spontaneous tumours in humans (p. 336, column 1). Phillips P ((Jun. 1998) JAMA, Vol. 279(24): 1936-7) further support the unpredictability of the state of the art by stating that a potential downside to inhibiting angiogenesis....the greatest potential concern is that inhibition will have an impact on normal physiological processes and

will have an impact on the female reproductive cycle, noted by James M. Pluda, MD senior clinical investigator in the Investigational Drug Branch of the National Cancer Institute (NCI). A second potential concern is that impact of angiogenesis inhibition on wound healing because new blood vessels must be created to heal wounds (p.1936, column 2, paragraph 2-8). Phillips P continues to state that the field of cancer is littered with drugs that have activity in mice that didn't translate into activity in people (p. 1936, column 2, paragraph 1).

With regards to extrapolating from *in vitro* data of the specification to gene therapy of a disease, the importance of relevant animal models for support of enablement is imperative in the determination for effectiveness of gene therapy. This observation is supported by Orkin et al. in the "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" (see pages 10-11 and 14). On page 11, second and third paragraphs, Orkin et al emphasize the importance of relevant animal models, and state that many "mouse models often do not faithfully mimic the relevant human conditions." Orkin et al also indicated that when dealing with cancer, the relevance of animal models appears to be less predictive than with other single-gene disorders. Note that the expression levels have not been demonstrated with regard to rendering treatment to a model for cancer. Even so, many other diseases and/or disorders (which are encompassed within the broad claims) require that the therapeutic gene be targeted to specific cells and/or tissues in order to achieve a therapeutic result. The specification fails to teach any specific parameters or conditions under which cell targeting can be predictably achieved. Yet, Orkin et al supports and discusses that cell targeting methodologies have not reached clinical

application and that research in these areas within the context of gene therapy strategies is in its infancy. See page 8, last paragraph and paragraph bridging pages 9-10. Miller et al. (The FASEB Journal, 1995) review the types of vectors available for *in vivo* gene delivery and conclude that, "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances...targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Moreover, Ledley (Pharmaceutical Research, 13: 1595-1614, 1996) states that the effectiveness of gene delivery *in vivo* is poorly predicted by *in vitro* results. Reasons why *in vitro* results would not be recapitulated *in vivo* include various biological barriers that are not reflected in *in vitro* models, and interactions between DNA or formulated DNA complexes with serum and blood elements (see page 1603, right column). In the instant application, the specification provides no teachings on parameters for which vectors can be targeted to which cells. Therefore, even if the specification enabled the construction of the gene delivery vehicle targeted to *in vitro* cellular modification, in the absence of particular guidance, the artisan would have been required to develop *in vivo* means of practicing the claimed methods; such unpredictable gene delivery art would have been considered to have necessitated undue experimentation on the part of the practitioner.

Furthermore, Eck & Wilson (The Pharmacological Basis of Therapeutics, 1996) support the importance of tailoring a gene therapy vector and method to specific diseases and/or disorders and not to all diseases and disorders. For example, Eck & Wilson et al review the state of the art

for gene therapy for inherited disorders and discloses that "[t]he level of protein function necessary to achieve complementation of the defect varies widely among genetic diseases." In particular, Eck & Wilson disclose that CFTR gene expression necessary to achieve therapeutic benefit is not known and the excessive production of an unregulated gene encoding α or β-chain of hemoglobin may result in more harm to the host than the disease itself (see page 78, column 2, Inherited Disorders).

With respect to enablement of claims directed to gene therapy or treatment, as this is an unpredictable art, a clear correlation to achieving therapeutic expression as broadly claimed must be provided by the specification. With regard to *in vivo* gene expression, Eck & Wilson go on to report that numerous factors complicate *in vivo* gene therapy with respect to predictably achieving levels and duration of gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, *etc.*), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. See page 82, column 1, first paragraph. These factors differ dramatically based on the route of administration of the vector, the protein being produced, and the disease and/or host being treated. As such, the specification fails to provide guidance for any of the above

parameters for *in vivo* gene expression nor do they provide a clear correlation to carrying out methods for therapeutic gene transfer protocols as broadly claimed.

Thus, the cited prior and post-filing art clearly indicates an unpredictable status of the gene therapy art. And, although, specific vectors, promoters, genes, and routes of administration might be or may have been effective for treatment of a specific disease providing a specific therapeutic effect, gene therapy as a broad-based art is clearly unpredictable in terms of achieving levels and duration of expression of a gene of interest which results in a therapeutic effect.

The claims are extremely broad, encompassing any and all routes of administration of an adenoviral vector comprising any and all DNA encoding endostatin in any and all host, and achieving "treatment" via gene therapy of any and all types of tumor or tumor metastases. The courts have stated that reasonable correlation must exist between scope of a right to exclude a patent application and scope of enablement set forth in patent application. 27USPQ2d 1662 *Ex parte Maizel*. Scope of Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). In view of the quantity of experimentation necessary, the lack of direction or guidance provided by the specification, the absence of working examples for the demonstration or correlation of an adenoviral vector delivery of endostatin to treating tumors as claimed, the unpredictable state of the art with respect to the expression of gene transfer, stability of mRNA, targeting capabilities and breadth of the claims to a method of treating by any and all routes of administration of an adenoviral vector comprising any and all DNA encoding endostatin, and achieving "treatment" via gene therapy of any and all types of tumor and tumor metastases, it

would have required undue experimentation for one skilled in the art to make and/or use the claimed inventions as broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 6, 11, 13-14, 16, 21, 23 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172-01. The omitted step is: the mere administration of the adenovirus does not lead to expression such that the final step is commensurate with the preamble which recites "a method of expression....." It is further pointed out that the claims are vague and indefinite as it is confusing as to what is considered the final result of performing the final step, i.e., adenoviral vector to expressing endostatin, in particular with regard to claims 4 and 28. Note that claims 5-10 depend from claim 4 and claims 29-31 depend from claim 28.

Claims 11, 14 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172-01. The omitted step is: the mere administration of the adenovirus does not

lead to treating tumor or a therapeutic effect such that the final step is commensurate with the preamble which recites "a method of treating tumor....." It is further pointed out that the claims are vague and indefinite as it is confusing as to what is considered the final result of performing the final step, i.e., adenoviral vector to encoding endostatin for the treatment of tumor, in particular with regard to claims 11, 14 and 21. Note that claims 12-13 depend from claim 11, claims 15-20 depend from claim 14 and claims 22-27 depend from claim 21.

Claims 6, 13, 16 and 23 are vague and indefinite for its recitation of "regionally" because it is unclear as to what area is encompassed within the claim as regionally administered or not regionally administered of the adenoviral vector. Does administered regionally mean at or around the site of the tumor? The metes and bounds of the claim cannot be determined.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-2, 4-7, 11-17, 21-24 and 28-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Leboulch et al (WO 99/264480).

Leboulch et al disclose a method for inhibiting tumor growth in a human patient harboring a solid tumor wherein said method comprising administering to said patient a nucleic acid molecule which expresses in said patient an anti-angiogenic polypeptide selected from the group consisting of human angiostatin, murine angiostatin, human endostatin, murine endostatin, and angiogenesis-inhibiting fragments thereof, wherein expression of the anti-angiogenic polypeptide in the patient inhibits angiogenesis in the vicinity of the tumor and/or systemically by diffusion of the recombinant protein to the vascular compartment from secreting transduced cells, thereby inhibiting its growth. Leboulch et al disclose several viral and liposome complex delivery methods including an adenoviral vector to mediate the gene delivery of nucleic acid encoding anti-angiogenic polypeptide. Leboulch et al further disclose gene delivery of choice will depend on such factors as the intended target and the route of administration, e.g., locally or systemically and the target can be, e.g., the peritoneal cavity, gastro-intestinal tract, bone marrow cavity, liver, lungs, muscles, vasculature, pericardial cavity, pleural cavity, skin, sub-cutaneous or deep connective tissues, central nervous system, spinal fluid, eye, or specific sites of tumor growth (p. 13-14). Thus, Leboulch et al clearly anticipated claims 1-2, 4-7, 11-17, 21-24 and 28-29 of the instant invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leboulch et al (WO 99/26480) taken with Blezinger et al (Apr. 1999) Nature Biotechnology, Vol. 17: 343-348.

Leboulch et al disclose a method for inhibiting tumor growth in a human patient harboring a solid tumor wherein said method comprising administering to said patient a nucleic acid molecule which expresses in said patient an anti-angiogenic polypeptide selected from the group consisting of human angiostatin, murine angiostatin, human endostatin, murine endostatin, and angiogenesis-inhibiting fragments thereof, wherein expression of the anti-angiogenic polypeptide in the patient inhibits angiogenesis in the vicinity of the tumor and/or systemically by diffusion of the recombinant protein to the vascular compartment from secreting transduced cells, thereby inhibiting its growth. Leboulch et al disclose several viral and liposome complex delivery methods including an adenoviral vector to mediate the gene delivery of nucleic acid encoding anti-angiogenic polypeptide. Leboulch et al further disclose gene delivery of choice will depend

on such factors as the intended target and the route of administration, e.g., locally or systemically and the target can be, e.g., the peritoneal cavity, gastro-intestinal tract, bone marrow cavity, liver, lungs, muscles, vasculature, pericardial cavity, pleural cavity, skin, sub-cutaneous or deep connective tissues, central nervous system, spinal fluid, eye, or specific sites of tumor growth (p. 13-14). Leboulch et al disclose a signal polypeptide and/or export signal is 5' (i.e., upstream) of the nucleotide sequence encoding the anti-angiogenic polypeptide and that the gene therapy vector has a nucleotide sequence encoding polypeptide and/or export signal which effects folding and secretion of the anti-angiogenic polypeptide *in vivo* (p. 9) i.e., PAP (plasminogen preactivation polypeptide and/or export signal). Leboulch et al differ from the claims in that the reference fails to disclose that a DNA sequence specifically encoding Ig-Kappa signal peptide immediately 5' to said DNA sequence encoding endostatin. However, the secondary references, Blezinger et al, cure the deficiency. Blezinger et al disclose the therapeutic potential of murine endostatin with a coding sequence for secretion signal from the mouse immunoglobulin Kappa chain for inhibition of tumor metastases and tumor growth and that to realize the therapeutic potential, alternative modes of targeting or efficiency in delivery are needed. Blezinger et al disclose a non-viral systemic inhibition of tumor growth and tumor by intramuscular administration of the endostatin gene with coding sequence for a secretion signal from the mouse immunoglobulin kappa chain and an epitope tag derived from influenza virus hemagglutinin A (Igk-HA) were fused to the N-terminus (p. 343, column 1-2) with a synthetic polymer called PINC for gene delivery to muscle tissue. It would have been obvious to one of ordinary skill in

view of the teachings of Blezinger et al to incorporate the Ig-kappa (mouse) secretion signal peptide immediately 5' to the DNA sequence encoding endostatin into an adenoviral vector to support the folding and secretion of the murine endostatin *in vivo*.

Accordingly, the modification of the secretion signal peptide of Leboulch et al by incorporating the Ig-Kappa signal peptide as suggested by Blezinger et al in order to obtain a recombinant adenoviral vector comprising a mouse, Ig-Kappa secretion signal peptide immediately 5' to the DNA sequence encoding murine endostatin was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 4, 7-10, 14, 18-20, 21, and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leboulch et al and Blezinger et al as applied to claim 1-3 above, and further in view of O'Reilly et al (U.S. Patent #5,854,205). Leboulch et al and Blezinger et al fail to teach a dosage for the administration of adenoviral vector in an effective amount to provide expression of endostatin in an amount of up to 1,000,000 ng/ml, at least 200 ng/ml, and from about 200 ng/ml to about 500 ng/ml for treatment of tumors or tumor metastases. O'Reilly et al disclose an endostatin therapeutic effective dosages for treatment of tumors in a mouse i.e., 20 mg/kg/day of recombinant mouse endostatin when tumors were approximately 200mm$^3$ (column 5). O'Reilly

et al further disclose that mouse endostatin was administered at either 20 mg/kg/day or 2.5 mg/kg/day, and human endostatin was administered at 20 mg/kg/day (column 6). One of ordinary skill would have been motivated to administered a variation of dosages of adenoviral vector of Leboulch et al and Blezinger et al in an effective amount to provide expression of endostatin to inhibit tumor growth and metastases.

Accordingly, the modification to the adenoviral vector of Leboulch et al and Blezinger et al by varying the dosage for viral administration as suggested by O'Reilly et al in order to effectively treat tumor growth and metastases was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the level of expression of the claimed invention. Therefore, the invention as a whole is *prima facie* obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leboulch et al and Blezinger et al as applied to claim 1-3 above, and further in view of Kovesdi et al (U.S. Patent #5,851,806). Leboulch et al and Blezinger et al fail to teach a method of expressing endostatin in mammalian cell, especially A549 or Hep3B cell. Kovesdi et al disclose generation of complementing cell lines using the cell line A549 as the parental line because transformation of A549 cells will yield a complementing cell line (similar to 293), wherein additional expression cassettes can be introduced, in a manner similar to that described for the 293 cell, to produce

multicomplementing cell lines with excellent plaqueing potential (column 21, example 8). Thus, it would be obvious to one of ordinary skill in the art to optimize production of adenovirus comprising a DNA encoding endostatin with either A549 or Hep3B cells as complementing cell.

Accordingly, the adenoviral vector of Leboulch et al and Blezinger et al by producing an alternative multicomplementing cell lines of A549 or Hep3B as suggested by Kovesdi et al in order to obtain a complementing cell lines for optimization of adenovirus production was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious, as evidenced by the references, especially in the absence of evidence to the contrary.

## *Conclusion*

**No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gai (Jennifer) Mi Lee, whose telephone number is 703-306-5881. The examiner can normally be reached on Monday-Thursday from 8:30 to 5:00 (EST). The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached on 703-308-2035. The FAX phone numbers for group 1600 are 703-308-4242 and 703-305-3014.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

**Gai (Jennifer) Lee**
**Patent Examiner**
**Art Unit 1600**

Jasemine C. Chambers

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